REMARKS

Reconsideration of this application, as amended, is respectfully requested.

Claims 14-17 and 19-30 were pending in this application. Claims 19, 27 and 30 were cancelled and the remaining claims were amended to further clarify the invention. No new matter is believed to have been introduced into the application as a result of the present amendment. Claims 14-17, 20-26, 28 and 29 are now pending in this application.

Consideration and entry of this amendment is respectfully requested. The Applicant believes that the claim amendment and the discussion below do not raise new issues for further consideration or require further search by the Examiner. Moreover, the Applicant believes that the amendments place this application into condition for an allowance or in better form for consideration on appeal.

Turning to the Office action, claims 14-17 and 19-30 were rejected under 35 USC § 112, second paragraph, for alleged indefiniteness. Claims 14-17 and 19-30 also stand rejected under 35 U.S.C. § 102(a) as being anticipated by Ge et al. (*J. Bacteriology*, Jan. 1997, pp. 552-556)("Ge (I)") and Ge et al. (*Infection and Immunity*, July 1997, Vol. 65(7), pp.2992-2995) ("Ge (II)"). Claims 14, 20 and 24 further stand rejected for the first time over Fikrig et al. (WO 97/42325)("Fikrig"). Applicants respectfully traverse these rejections.

The present invention, as claimed, relates to a diagnostic reagent for early detection of Lyme disease comprising recombinant FlaA protein, including amino acid sequences as shown in SEQ ID NO:2, antigenic fragments thereof sufficient to produce an immunogenic response, and a fusion protein. The invention, as claimed also relates to a diagnostic reagent for early detection of Lyme disease comprising recombinant FlaA protein produced by an expression method that employs freshly transformed host cells. The use of fresh transformant colonies in the method, surprisingly, results in the successful expression of FlaA protein. In contrast, cells propagated from subculture produced little or no recombinant protein in the expression system. See the specification at pages 5, line 1 to page 6, line 15, and page 13, lines 1-7.

Rejection under 35 USC §112, second paragraph

The Examiner has rejected claims 14-17 and 19-30 under §112, second paragraph as being vague and indefinite with regard to the recitation of "recombinant FlaA or P37 protein". As the Examiner has keenly recognized, there is ambiguity regarding the use of P37 to describe two different proteins in *B. burgdorferi*. The term, "P37" has been used generally in the art to describe proteins having a 37kDa weight. Two 37 kDa proteins have been identified from the *B. burgdorferi* tick; a P37 protein isolated by Fikrig, et al. (*Immunity*, 6:531-529 (1997)) and the FlaA protein of the present invention. Recently, the confusion in terminology has been recognized in an article by Feng, et al. (*Infection and Immunity*, Vol. 68, No. 7, pp. 4172, 4169-4173 (July 2000)). In Feng, on page 4172, column 1, first paragraph of the Discussion, the author has clarified the misunderstanding in description of the 37 kDa protein from *B. burgdorferi* and has also distinguished the P37 and FlaA proteins. Applicants' invention concerns only a diagnostic reagent comprising the FlaA protein.

In order to minimize any confusion and to conform with currently defined terminology as provided by the Feng reference, the term "P37" has been deleted from the pending claims. Applicants' reference to a "P37" protein is in fact the FlaA protein as claimed and supported throughout the specification. A copy of the Feng reference is submitted herewith in an IDS under 37 CFR 1.97(d).

Rejection under 35 USC §102(a) in view of Ge (I) and Ge (II)

In response to the 35 USC §102(a) rejection of claims 14-17 and 19-30 under either of the Ge articles, and specifically the Ge (II) reference, the Examiner has improperly concluded that the prior art teaches the product of the present claims. Data in Ge (II) showing only 2 out of 19 patients (a mere 10%) positively reacted with the FlaA protein is insufficient data to anticipate FlaA as a diagnostic indicator of Lyme disease. On the contrary, the Ge (II) data demonstrating 90% of patients reacted negatively to FlaA is a significant teaching away from the use of FlaA as a diagnostic reagent. Ge (II) has acknowledged as much in the following sections of the reference:

(i) Ge (II) states in the abstract, p. 2992 that "immunoblotting with sera from mammalian hosts infected with *B. burgdorferi* indicated that FlaA is not an immunodominant antigen in Lyme disease."

(ii) Ge (II) declares in the last paragraph of p. 2994 that "*B. burgdorferi* FlaA does not appear to be a consistent immunodominant antigen in infected mammalian hosts. Therefore, although FlaA is a protein unique to spirochetes, our results suggest that it is not a good candidate for the diagnosis of Lyme disease."

The Examiner has misconstrued what the reference and data teach and improperly disregarded what is claimed in the present invention. The Ge(II) reference only represents, by the author's admission, that FlaA is antigenic and can be expressed *in vivo*. The fact that this work failed to teach and in fact taught away from the use of FlaA as a diagnostic reagent makes it highly uncertain that one of ordinary skill at the time would have seized on the one sentence in that article that the Examiner emphasizes. (*U.S. v. Telectronics*, 2 USPQ2d 1571 (DC Colorado 1987)).

The Ge (I) reference also does not teach a diagnostic reagent as claimed in the present invention. Neither the Ge(I) or Ge(II) references can be properly used as anticipatory prior art and the §102 rejection under either reference cannot stand.

Further, to be considered anticipatory under §102, identity of all elements of a claim must be fully met in one reference in order to sustain an anticipation rejection. (See, *Kalman v. Kimberly-Clark Corporation*, 218 USPQ 781, 789 (CAFC 1983). Although a limitation is found in the preamble, effect is given to the preamble if it is "necessary to give life, meaning and vitality" to a claim (*Kropa v. Robie*, 88 USP 478, 480-481 (CCPA 1951)). Anticipation was not found in a case where without the essential limitations in the preamble of the claim, the structures of the claim alone did not define the invention and the problems solved by the inventors. (*Corning v. Sumitomo*, 9 USPQ2d 1962, 1966 (1989)).

The present claims as amended set forth a diagnostic reagent for detecting Lyme disease. The problem solved by the inventors lies in the effective use of the FlaA protein as the diagnostic reagent. Without this limitation, the scope of the claims in the context of the problem

Ge references. Thus, the Examiner has not shown identity of all elements of the present claims in the Ge references. In view of the technical arguments and legal arguments, the Examiner has not met her prima facie burden to sustain a rejection under 35 USC §102(a). Accordingly, withdrawal of the 35 USC §102(a) rejection based on Ge (I) and Ge (II) is in order and is respectfully requested.

Rejection under 35 USC §102(a) in view of Fikrig (WO 97/42325)

In response to the Examiner's rejection of claims 14, 20 and 24 under 35 USC §102(a) as being anticipated by Fikrig (WO 97/42325), the claims have been amended deleting the term "P37", therefore, the rejection is now moot. The P37 protein of Fikrig is not the same as the 37 kDa FlaA protein of the present invention. The P37 nucleic acid sequence of Fikrig (SEQ. ID. NO.:6) is not the same or complementary to the FlaA sequence of the present invention. Accordingly, withdrawal of the 35 USC §102(a) rejection of claims 14, 20, and 24 is in order and is respectfully requested.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned representative if the Examiner believes this would be helpful in expediting prosecution of this application.

Respectfully submitted,

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APPENDIX A

14. A diagnostic reagent for early detection of Lyme disease comprising a recombinant FlaA protein.

15. The diagnostic reagent of claim 14, wherein said recombinant protein comprises an amino acid sequence as shown in SEQ ID NO.:2 and antigenic fragments thereof sufficient to produce an immunogenic response.

16. The diagnostic reagent as in claim 15 wherein said recombinant FlaA protein comprises a fusion protein.

17. The diagnostic reagent as in claim 16 wherein said fusion protein is approximately a 38 kDa T7 gene 10 product.

20. A diagnostic reagent for early detection of Lyme disease produced by a method comprising: providing freshly transformed host cells; constructing a DNA expression vector containing an expressible FlaA encoding DNA sequence; transforming a suitable host cell with said expression vector; plating out said transformed host cells; preparing large scale primary cell cultures from transformed host cells taken from a fresh transformant colony; and inducing FlaA protein expression from said host cells in culture to produce a recombinant FlaA protein.

21. A diagnostic reagent as in claim 20 wherein said diagnostic reagent is encoded by a nucleic acid sequence as shown in SEQ ID NO: 1.

22. A diagnostic reagent as in claim 20 comprising an amino acid sequence as shown in SEQ ID NO: 2 and antigenic fragments thereof sufficient to produce an immunogenic response.

23. A diagnostic reagent as in claim 20 further comprising amplifying a nucleic acid sequence encoding an FlaA protein with nucleic acid primers selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6 and complementary sequences thereof.

24. A diagnostic reagent as in claim 20 wherein said recombinant FlaA protein is a fusion protein.

gene 10 product.

26. A diagnostic reagent as in claim 20 wherein said transformed host cell is an E. Coli cell.

28. A host cell containing the nucleic acid sequence of claim 21 or a complement thereof.

29. An expression vector comprising the nucleic acid sequence of claim 21 or a complement thereof.